ON THE SIGNIFICANCE OF JAUNDICE IN TYPHOID FEVER, AND ON THE HEPATIC COMPLICATIONS WITHOUT JAUNDICE.

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During the past winter there were in the wards at the Pennsylvania Hospital a number of cases of typhoid fever that presented the peculiar and rare symptom, jaundice. It is the object of this paper to analyze these cases and to inquire into the significance of jaundice when occurring in typhoid fever, at the same time that the hepatic complications in which jaundice does not generally happen will be passed in review.

Case I.—A colored woman, aged eighteen years, was in the ward for a long time, extremely ill with typhoid fever. The course of the fever was marked by only moderate diarrhœa, but it was attended with very high temperature, the record showing temperatures of 105° and upward, and by nervous manifestations, especially delirium; the Widal reaction was decided. In this case of long-continued typhoid fever there appeared two striking symptoms: one was jaundice, the second was inflammation of the right parotid gland.

The jaundice appeared on the eleventh day of the disease, and though by the thirtieth it had greatly diminished, yellowness was still perceived in the conjunctivæ. The jaundice was not associated with any marked change in the size of the liver; if there were any, it was slightly increased, for the percussion dulness was distinctly to be detected below the margin of the ribs; the organ was painful to the touch when pressure was made over its free border, and there was general sensitiveness of the abdomen.

Subsequent to this state of things the right parotid gland gave evidence of inflammation, and became tumid and tender. The swelling at the angle of the jaw subsided without suppuration under local treatment with ice and applications of tincture of iodine, and by the thirtieth day of the disease there was very little to be felt of the parotid swelling, which at one time threatened to form an abscess. As further symptoms in the case may be noted nausea and vomiting, hebetude, and albuminous urine showing blood-cells and granular and hyaline casts, as well as pus casts and bile-stained

epithelial cells. The urine was freely passed, forty-six ounces in twenty-four hours, and contained one-half gramme of albumin to the litre; it responded readily to the tests both for biliverdin and bilirubin. On several occasions chills occurred, but they were not severe; the blood was examined for malarial organisms, with negative results.

Jaundice persisted, though slight, for a few days more; the tenderness over the lower part of the liver disappeared; the bowels were constipated; the tongue was somewhat coated; the temperature was 99°. The urine, tested repeatedly when the jaundice was at its height, gave evidence of the presence of bile-pigment. The stools were never clay-colored; indeed, they were usually the ordinary stools of typhoid fever; sometimes they were noted as brown, sometimes as yellow or greenish. No bile-pigment was detected in the urine on March 7th, the thirty-second day of the disease. The patient made a good, though slow, convalescence.

It is worthy of note that the jaundice was associated with parotid swelling, which I think more than a coincidence, as it has happened in other instances, as we shall further on see.

Let me now give the particulars of a case of jaundice in typhoid fever which came on very late in the disease, only three or four days before death, and grew in intensity to the fatal ending.

Case II.—Sarah K. B., aged thirty years, white, was admitted February 18, 1898, with the statement that thirteen days previously she had been taken ill with anorexia, diarrhœa, vomiting, and epistaxis. She had not had a chill, headache, or cough. Upon admission her temperature was 104°, the pulse 120, the respirations were 40 to the minute. Her cheeks were flushed, the pupils were large, the sclera clear, the conjunctivæ of a good color. Sordes existed upon the teeth and lips. The tongue was dry, red at the tips and edges, with a brown streak in the centre. Her breath was fetid. The lungs were clear on percussion; there were no râles. At the apex of the heart was heard a blowing systolic murmur, not transmitted; at the base, too, was a soft, blowing systolic murmur, which was transmitted into the carotids; there was no venous hum. The heart's action was regular but rapid. The pulse was small in volume and dicrotic. The liver-dulness began at the sixth rib and extended to the costal margin; the border was not palpable. The spleen extended from the eighth rib in the mid-axillary line to the last rib; it was not palpable, and not tender upon percussion. The abdomen was tympanitic, and, upon pressure, pain and gurgling were elicited in the right iliac fossa. Characteristic rose-spots were found on the abdominal surface. There were pre-tibial œdema and some pain upon pressure in the legs.

On the following day it was noted that hebetude was marked, the facial expression was dull, the temperature was 102° to 103°, the pulse very weak, dicrotic, and compressible. The urine was straw-colored, with an abundant sediment; it was acid, of specific gravity 1030, and contained a trace of albumin, with abundant urates and granular and hyaline casts.

The treatment was beta-naphtol, three grains every third hour; whiskey, a half-ounce every second hour; strychnine sulphate, one-thirtieth of a grain every fourth hour, and a milk diet. The surface of the body was sponged with cold water every third hour, when the temperature was 103° or over.

During the next few days the bowel movements continued loose and frequent, from four to seven daily. The eruption became more profuse. The temperature was only kept down by systematic sponging. The splenic area of dulness became much increased, and some local tenderness developed; the tongue became dry, brown, and fissured. The Widal test of the blood yielded a positive reaction. The stimulant was increased to five drachms every two hours on the 21st, on account of the very dicrotic character of the pulse; but as this was better the next day the whiskey was decreased to four drachms every two hours. The hebetude continued; there was epistaxis on the 23d. On the 24th the pulse was noted as stronger and more regular, though still rapid. A systolic murmur, looked upon as hæmic, persisted. There was marked throbbing of the carotids; the second cardiac sound was distinct. She was weak and exhausted, at times delirious, though the mind was mostly clear. On the 25th some yellowness of the conjunctivæ was observed, and the urine contained bile-pigment. On the 26th it was noted that the skin and conjunctivæ were markedly jaundiced. The pulse was feeble and compressible. The bowels were very loose, eight movements within the last twenty-four hours, notwithstanding the use of opium suppositories; the discharges were thin and yellow. Dilute nitro-muriatic acid, fifteen minims, was given every four hours in place of the beta-naphtol, which had been discontinued. Oxygen inhalations were also employed, and she took strychnine.

On the 28th the records state that the delirium was deepening. She was intensely jaundiced all over the body. The eruption was still profuse; the liver was not enlarged or palpable; there was no pain or soreness over it. The pulse was very weak; sordes were present on the teeth and tongue; the bowel movements were green and yellow, and still loose. In spite of very free stimulation, the patient died of exhaustion during the evening. An autopsy was not obtained.

In the cases that have been detailed the jaundice occurred as a late symptom. Jaundice may be, however, an early symptom, and even show itself in advance of the fever, appearing as the result of an early infective process in the bile-ducts.

In a remarkable case which, so far as I know, is unique, the jaundice distinctly preceded the development of the typhoid fever, and occurred during the latter part of the period of incubation.

Case III.—A Danish weaver was admitted into my ward at the hospital on January 7, 1884. He had been jaundiced for a few days without obvious cause. He complained of weakness and loss of appetite. His temperature was 99.5°, the pulse 118. The next day the yellowness of the conjunctivæ

and the skin was more marked; the tongue had a heavy yellow coat; the liver was observed to be somewhat enlarged, as was the spleen. The case was looked upon as one of catarrhal jaundice, and he was treated with phosphate of sodium and Rochelle salts, and placed on a restricted diet. The jaundice slowly improved and almost passed away, but the man did not get well, for, after the 19th, he was noticed to be decidedly feverish, and on the 24th the morning temperature was 104°, and he was very weak; his face was flushed; diarrhœa set in. A note made at this time states that he had all the appearances of beginning typhoid fever. On the 27th there was no doubt of the correctness of this view. The tongue was coated, with red edges and tips. The abdomen was tympanitic, the movements from the bowels loose and of typhoid character. Rose-colored spots were found on the abdomen. He had repeated epistaxis.

He was treated with eight grains of quinine daily, with stimulus, with dilute muriatic acid, and, later, with turpentine. In the course of the case great restlessness, delirium, and subsultus tendinum were noted, followed by marked hebetude, increasing prostration, and frequent involuntary movements from the bowels. He died February 4th, from exhaustion.

At the autopsy the liver was found to weigh four pounds, eight ounces. The gall-bladder contained thin, pale-colored bile; there was no evidence of inflammation or ulceration of its mucous membrane, or of disease of the bile-ducts. The hepatic cells showed a cloudy swelling; the same condition was noticed in the epithelium of the kidneys, which were otherwise healthy. The spleen weighed twenty ounces, was highly congested, and its tissues soft. The posterior portions of the lungs were much congested. A number of infiltrated and ulcerated Peyer's patches were found in the lowest part of the ileum. There was also ulceration of many of the glands of the large intestine, and considerable swelling of the glands of the mesentery.

It is difficult in this case to state exactly when the typhoid fever began, but, counting from the appearance of the eruption, which we know to be between the seventh and ninth days, the fever probably started on the 18th or 19th of January, and thus about two weeks after the onset of the jaundice. This, therefore, would be strictly within the period of incubation, and it seems reasonable to suppose that the typhoid infection had lighted up a catarrhal process in the gall-bladder and bile-ducts which antedated the intestinal affection and disappeared in the course of the febrile malady. The alternative suggestion is coincidence, which seems very unlikely.

The case of jaundice in typhoid fever that I shall now describe was admitted into the Pennsylvania Hospital on January 31, 1898, the day on which I gave up the men's medical ward to my colleague, Dr. Arthur V. Meigs, who kindly permits me to give the details of the case as it developed under his observation.

CASE IV.—J. S , a waiter, aged twenty-six years, was admitted into the hospital with the distinct statement that he had never had pneumonia, an affection of the liver, rheumatism, or typhoid fever. He had been ill for ten days previous to admission, and a week before his admission he was seized with a severe chill, followed by fever, sweats, and epigastric pains. From this time on he had a number of chills, with severe abdominal pains, most acute over the region of the gall-bladder, accompanied by obstinate constipation and vomiting. When examined on admission his temperature was 102.2°, the pulse 88; the skin and conjunctivæ were decidedly jaundiced; the tongue was heavily coated; the abdomen rigid, not distended, but generally painful on percussion. There was no particular tenderness in the right iliac fossa; the greatest tenderness was over the region of the gall-bladder, and pressure there caused nausea. The liver was distinctly enlarged and palpable. A considerable amount of urine was drawn by catheter. The man lay in bed with his legs flexed and with all the appearances of a local peritonitis. Poultices were applied to the abdomen without material modification of the symptoms. On the evening of the first day the temperature attained to 104.4°. It declined to 98.6° the next morning, and then passed by evening to 103°. On the second day after admission it had fallen early in the morning to 99°. The patient was extremely restless, with clammy perspirations, the pulse was imperceptible, and he soon died.

His case suggested an inflammatory disease within the abdomen rather than typhoid fever, and the symptoms were such as might have been due to an appendicitis at the upper part of the appendix.

At the autopsy typical typhoid ulcers were found in the ileum and cæcum, the mesenteric glands were swollen, the spleen was large and friable; there was no peritonitis. The liver was considerably enlarged; its left lobe had a blunt edge. There was no abscess or gross lesion in the liver. The gall-bladder was distended with an unhealthy-looking bile; it contained no concretions; its coats were not altered; it had no adhesions. There was no swelling or sign of inflammation in the biliary ducts. The base of the right lung was congested.

It appeared at first from the symptoms that the case was one of cholecystitis; the nausea and vomiting, and especially the seat of pain, pointed to it. But the autopsy did not bear out this view, since no signs of inflammation of the gall-bladder were found. The distention of the viscus was the only thing to account for the pain; and the jaundice must, after all, have been the result of the blood alteration and the morbid condition of the liver structure. It is to be regretted that there are no microscopical or bacteriological examinations to record.

In the case we have just examined the jaundice was associated with the occurrence of chills; indeed these formed a prominent feature of the morbid manifestations. They were yet more so in the following case, though the lesion was, I believe, a different one. The man was

shown at a clinic with great enlargement of the spleen in the course of typhoid fever, and the jaundice subsequently developed in the midst of very grave symptoms.

Case V.—A Swedish sailor, aged twenty-three years, was admitted on December 6, 1897, with severe abdominal pain, that was at first over the whole upper part of the abdomen, but had localized itself in the left hypochondrium, extending almost to the crest of the ileum. The temperature was 99.6°. The bowels were moved two or three times daily; the discharges were not loose. The pulse was 120, weak, and irregular; the tongue markedly coated and tremulous. The history obtained was that he had been an unusually healthy man who did not remember any illness except an attack of malaria some years ago. Eight weeks since, while at sea, he began to suffer with headache and weakness; subsequently was seized with fever; was delirious part of the time, and altogether decidedly ill for weeks on board ship. He was very weak when he left the ship, but after reaching land he began to improve until the last few days, when he had night-sweats, abdominal cramps, and felt himself very ill. The day of admission the temperature rose in the evening to 104.2°; no rose-spots were found. The most marked feature of the case was the extent of the splenic dulness, which was 18 cm. in length from the sixth rib laterally, and passed fully two fingers'-breadth below the costal margin. The enlarged organ could be distinctly felt, and was very tender on pressure; indeed, the whole splenic region was tender to the touch, extremely so on percussion. Bulging was visible to the eye, and the line of dulness was influenced by inspiration and expiration. The heart's action was rapid, the second sound accentuated; there was no murmur; marked pulsation existed at the supra-clavicular notch.

He was looked upon as having typhoid fever with splenitis, and the question of abscess of the spleen was considered. There was some doubt whether we were dealing with the primary attack of the fever, prolonged by the condition of the spleen, or with a relapse; the former view was adopted. The patient was placed on dilute muriatic acid, twenty minims every fourth hour, on milk-diet, and the ointment of iodide of mercury and lanolin, equal parts, with four grains of extract of belladonna, was rubbed in over the spleen. The blood examined microscopically showed 4,500,000 red to 6000 white corpuscles. Widal's reaction was positive. The urine was acid, of specific gravity 1029, and contained neither sugar, nor albumin, nor casts.

On December 9th, three days after admission, a crop of rose-spots was found on the abdomen. These disappeared by the 13th; his whole condition was steadily improving and the temperature had become normal A note on the 16th speaks of the large size of the spleen persisting, but of the tenderness having gone; of the absence of tympany, of tension of the abdomen, and of any signs of cardiac disease. On the 17th the temperature began to rise, and by the evening of the 18th it had attained to 105°; the pulse was 148, and weak; the respirations were 40. There was a slight return of the splenic tenderness, but nothing marked. The blood was examined for plas-

modium; none was found. Dark days followed, with recurring severe chills and temperature of 106°, with a pulse weak and 156; with hurried, shallow breathing and congested lungs, but with the murmur remaining vesicular. The first sound of the heart was indistinct, the second clearer and well defined. In the blood, repeatedly examined, no plasmodium was detected; a repetition of Widal's test gave again the same positive result. Quinine in large doses produced no effect on the chills, and but little on the temperature. A cold bath reduced it to 95°, but he did not bear the bath well. The temperature rose again by the next day to 105.3°, and two chills happened on that day. After the chills and the fever rises the patient did not sweat, but the skin was moist. A note of the 21st mentions yellowness of the skin and the conjunctivæ, and bile in a urine free from sugar, but slightly albuminous and containing hyaline and granular casts. There was no distention of the gall-bladder; the lower border of the liver could be felt, and was slightly tender; the organ extended just below the margin of the ribs. General abdominal pain existed at the upper part of the abdomen; the stools were not clay-colored.

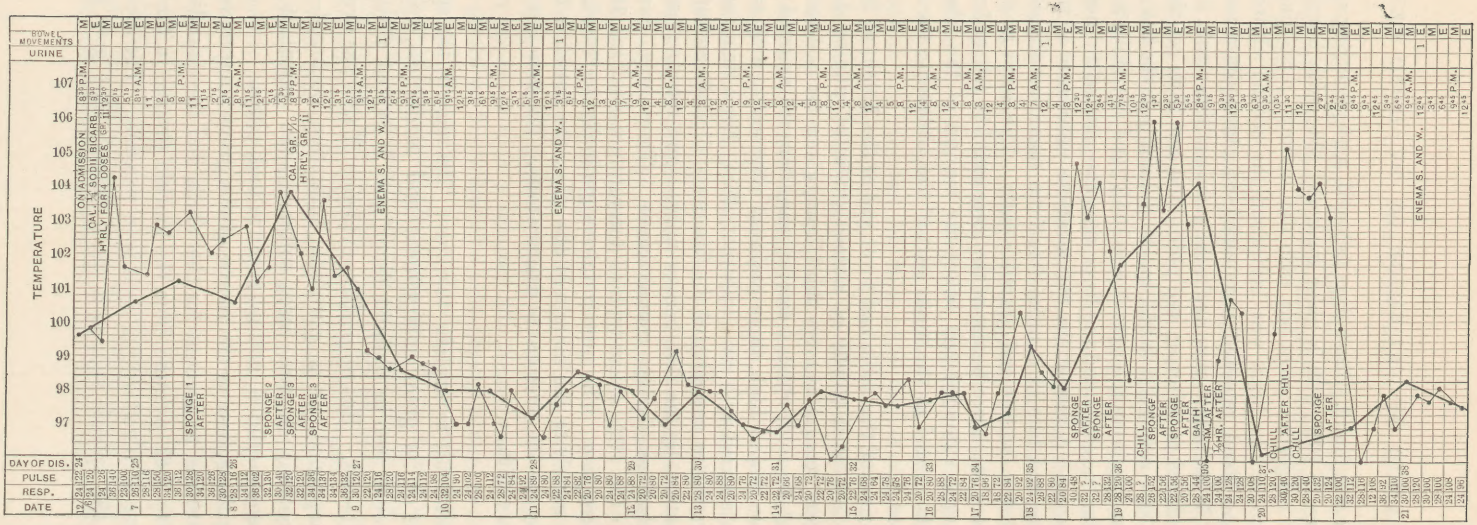
During the time of the chills and fever and at the height of the jaundice the treatment consisted chiefly of sixteen grains of quinine daily, and of borate of sodium, ten grains every third hour, given for a time in place of the dilute muriatic acid, which, however, was afterward resumed; and, while the temperature was so high, three grains of phenacetin, with two of salol, were also administered with some apparent effect. For a time, too, the weakness of the circulation necessitated the free use of digitalis and of whiskey.

The temperature, by the 21st, became normal and remained so with occasional exacerbations during convalescence. There was, however, from January 2d to the 10th, a post-typhoid temperature reaching 102°, without return of the eruption. The splenic dulness gradually decreased, and by the 5th extended merely to the margin of the ribs; the jaundice had entirely disappeared by the 5th, even to the urinary tests. The man left the hospital well on January 26th.

It is very difficult to explain this case. As regards the spleen, there was no doubt of its great enlargement and tenderness, more marked than I have ever seen in typhoid fever, and I looked throughout the case for an abscess. But no positive evidence of this was ever obtained, and if it happened, or a purulent infarction occurred—which, as Murchison noticed in two cases, softened—the purulent fluid was absorbed or encapsulated, and no rupture took place.

Regarding the spleen as the source of the grave symptoms, two views suggest themselves to account for the chills and the jaundice. One is that they were both pyæmic from the morbid process in the spleen, the jaundice being of blood origin, as it is in pyæmia. The second is that, considering the splenic vein as a main branch that goes to form the

Temperature Chart of Case V.



The lighter lines represent the intermediate temperatures.

portal vein, infected thrombi produced a pylephlebitis, and that chills and jaundice, the latter certainly, resulted from the superinduced condition of the portal vein. The difficulty of adopting this view is the recovery. Still, we know that pylephlebitis may end in recovery. Frerichs tells us that this may happen when the pylephlebitis is not too extensive. In a recent operation for typhlitis Treves[1] actually saw the morbid lesions. The liver surface was dotted over with the innumerable yellow specks regarded as characteristic of the disease, and the patient's condition appeared hopeless, but she recovered. On the whole, I believe that the view of the patient whose case I have been describing having had pylephlebitis is the correct one.

Jaundice is of very rare occurrence in typhoid fever. Sir William Jenner[2] states that he has never observed a case. Murchison[3] has met with it in but four instances, and had a fifth case communicated to him. My friend and late colleague at the Pennsylvania Hospital, James H. Hutchinson, reviewing his experience in typhoid fever in an excellent article,[4] mentions that he had not seen this complication. Petrina,[5] during the years 1875 to 1880, met with but one case in 194 deaths from typhoid fever. Griesinger is quoted by Liebermeister[6] as having noted it ten times in 600 cases, and Liebermeister mentions that in the hospital at Basle it was observed twenty-six times in 1420 cases, or one in about fifty-five. These figures indicate higher proportions than jaundice is generally regarded as occurring in, except in hot climates. Jamieson[7] states that in China it is generally, perhaps always, present to a greater or less extent in prolonged cases, and cites nine cases in which it was deep. But Sorel,[8] in Algeria, observed only six cases in 871 of typhoid fever. In cold climates jaundice in typhoid fever must be very rare. Huss,[9] in analyzing 2294 cases of typhus abdominalis—typhoid fever—in Stockholm, does not mention an instance. Yet Werner,[10] in St. Petersburg, speaks of having observed ten cases in one outbreak of typhoid fever.

Prior to this winter I had met with but a solitary instance that I can recall, and it is remarkable that this paper, which contributes five to the scanty general number, should record four observed in the last

[1] British Medical Journal, February, 1894.
[2] On Fevers and Diphtheria.
[3] Diseases of the Liver, 2d ed., 1877, p. 401.
[4] System of Practical Medicine by American Authors, vol. i. p. 295.
[5] Prag. med. Wochenschrift, 1881, No. 41–43.
[6] Ziemssen's Cyclopædia of the Practice of Medicine, vol. i.
[7] Imperial Maritime Customs, China Med. Reports, 1888–95, 37th Issue, pp. 63, 67.
[8] Bull. et Mém. de la Société Méd. des Hôpitaux de Paris, 1889, tome vi. 3d series.
[9] Statistics and Treatment of Typhus and Typhoid Fever, etc., 1855.
[10] St. Petersburger med. Wochenschrift, 1892, p. 32.

few months, during which we have had a widespread epidemic of typhoid fever in Philadelphia. Where there is a complication of malaria, jaundice is not infrequent. Thus, in the report of so-called typho-malarial fever from the Seminary Hospital during the civil war, jaundice occurred in seven out of 64 cases, only one case of which was fatal.

As regards the time of the occurrence of the jaundice, it generally does not come on until the middle of or until late in the disease. In my own cases, omitting Case III., where it antedated the febrile malady, it began in one case (Case I.) on the eleventh day; in Case II., on the twenty-third day; in Case IV. it probably came on in the first week; in Case V., as convalescence seemed to have been reached. In most of the instances on record that I have analyzed, it appeared in the second or third week of the disease. Still the jaundice may happen early, as it did in many of Jamieson's cases.[2] In one of Andral's fatal cases[3] it occurred on the third day; in a fatal case of Frerichs',[4] on the fifth; in one of Murchison's[5] that recovered, it appeared on the sixth day of a relapse; in one of Osler's[6] cases, also ending in recovery, on the fourth day of a relapse; in one of Sorel's[7] cases, not until convalescence; in McPhedran's case,[8] just before convalescence. It may go on, and is apt to go on, gradually deepening until death, and may—though this is very exceptional—become dark and intense. In cases that recover the jaundice gradually disappears with the fever; yet it may persist into convalescence, as in Case I. of this paper, and even remain after the patient is able to be about.[9]

With reference to the symptoms that attend the jaundice, we do not find that they are constant; they are, as a rule, the symptoms of a severe case of typhoid fever with the usual amount of tympany and nervous disturbance. Delirium is apt to be present; yet I cannot say that it has seemed to me much aggravated by the hepatic condition, and there are intervals of clear mind even in the delirious patients, as happened in Case IV. and in Case V., in which questions are answered rationally. The temperatures are, as a rule, high, and, as the cases here presented prove, chills are not uncommon; nor are pulmonary congestions. Vomiting is a frequent but far from invariable symptom.

[1] Medical and Surgical History. Medical History, part iii. p. 305.
[2] Loc. cit.
[3] Clinique Méd., 1834, vol. i.
[4] Diseases of the Liver, 1858.
[5] Diseases of the Liver, Case CXXXVII.
[6] Case I., Transactions of the Association of American Physicians, vol. xii., 1897, p. 380.
[7] Société Méd. des Hôpitaux, tome vi.
[8] Canadian Practitioner, March, 1891.
[9] Case XXXVIII. in Murchison, Treatise on the Diseases of the Liver.

The urine almost always contains bile, and, as in grave cases of typhoid fever, is apt to show some albumin and granular and hyaline casts. Examined by Murchison,[1] in two cases, for leucin and tyrosin, these were not found. The character of the stools is of special interest; they are much like the ordinary typhoid stools, or darker and greenish; they are very rarely clay-colored. In four of the five cases here reported they were not. But in one of Murchison's[2] cases in which jaundice happened during a relapse, the stools were noticed as clay-colored, and the same in Osler's[3] case in which jaundice appeared early in a relapse. There may be, as in one of Andral's[4] cases, marked constipation. Neither the temperature nor the pulse has appeared to me to be influenced by the occurrence of the jaundice; the temperature remains high, the pulse rapid. In some instances profuse sweats occur. The liver is generally somewhat sensitive to the touch, especially at its lower border. In the cases I have noted it was slightly enlarged or of normal size. But it has been observed to be much reduced, as in the case reported by Sabourin;[5] in the case mentioned by Frerichs, the hepatic dulness was almost absent.[6]

Complications attending the cases in which jaundice is met with are not unusual. Marked pulmonary engorgement existed in Cases IV. and V. detailed in this paper. In one of Andral's[7] cases the patient died of left-sided pneumonia on the ninth day of the disease; both lungs were highly congested. In a case described by Louis[8] in which jaundice and bilious vomiting occurred, there was a purulent swelling of the right parotid; abscesses were found in the liver. In the first case of my series there was also parotid swelling, but it did not suppurate. In Sander's[9] case double parotitis followed, and the number of cases of combination of jaundice with parotitis in typhoid fever shows that it is more than coincidence. In one of Frerichs' cases,[10] too, parotitis is mentioned, but it was associated with typhus rather than with typhoid, and, therefore, cannot be, strictly speaking, considered here. In another[11] of his cases of jaundice in undoubted typhoid, profuse epistaxis preceded the jaundice, as it did in Case II. of my series. In Lannois' case[12] the epistaxis was marked and repeated; the jaundice was very intense,

[1] Ibid., p. 420.
[2] Diseases of the Liver, Case CXXXVII.
[3] Loc. cit., p. 380.
[4] Clinique Méd., 1834, vol. i. p. 11.
[5] Revue de Médecine, 1882, p. 600.
[6] Observ. XVIII., Diseases of the Liver, vol. i., Sydenh. Soc. Trans., p. 215.
[7] Clinique Médicale, 1834, tome i. p. 11.
[8] Fièvre Typhoide, vol. i., Observ. XVII., p. 111.
[9] Deutsche Klinik, 1861, p. 70.
[10] Diseases of the Liver, p. 168.
[11] Ibid., Observ. XVIII., p. 215.
[12] Revue de Méd., 1895, p. 911.

black. Epistaxis, indeed, bears, I think, a distinct relation to the jaundice and its intensity. In one of Murchison's[1] cases thrombosis of the femoral vein happened in a patient who had become jaundiced on the fourteenth day of enteric fever. In Freundlich's case[2] thrombosis of the scrotal veins and gangrene of the left inguinal region coexisted. He had also double croupous pneumonia of the lower lobes. When jaundice is severe and occurs early, Jamieson[3] speaks of its usual association with hæmoglobinuria, intestinal hemorrhage, and hæmatemesis —indications of blood dissolution.

Having examined into the mode of appearance of the jaundice and the symptoms attending it, let us inquire into its origin. Is it a jaundice of obstruction to the flow of bile, such as we know catarrhal jaundice to be, or is it due to the blood condition and the changes in the parenchymatous structure of the liver? In the great majority of instances, most assuredly, I think, not to the former condition. It is usually a blood jaundice, with more or less disorganization of the red corpuscles and often associated with alteration in the liver cells. In favor of this view we have these facts: its occurrence, as a rule, as a late symptom and in grave cases; the character of the stools, which are but little modified, and do not show any hinderance to the flow of bile; the general similarity to the jaundice noticed in other infective diseases and altered blood states, such as in pyæmia. The condition of the liver itself does not give us much information. Yet where the organ has been carefully examined it has been found to show degeneration, granular or fatty, of the hepatic cells, that has even been likened by Frerichs to the state found in acute atrophy. Then in some instances we have abscess, though not in many, for I shall presently show that in the majority of cases abscess of the liver attendant on typhoid fever is not accompanied by jaundice. Further, we may have a pylephlebitis, with secondary changes in the hepatic tissue. However different, these causes may be all grouped together as non-obstructive jaundice—jaundice not from catarrhal obstruction of the bile-ducts. In a few instances this, however, does happen, and the records submitted in this paper prove that it is especially as a precursor to the active development of the enteric fever (as in Case III. of my own cases), or in the early stage of a relapse, that this kind of jaundice occurs.

Broadly speaking, then, the jaundice met with in enteric fever is due to the blood affection and the alterations produced by the toxins of the disease in the secreting cells of the liver, or to gross changes otherwise

[1] Diseases of the Liver, 2d ed., Observ. CXXIX., p. 420.
[2] Deutsche Archiv für klin. Med., Bd. xxxiii., 1883, p. 318.
[3] Loc. cit., p. 63.

there induced, and only in exceptional instances to a catarrhal condition of the bile-ducts. Besides this, jaundice in typhoid fever occurs from inflammation of the gall-bladder and the morbid changes in the bile-ducts that may attend the cholecystitis. But this I only mention here to enumerate all the causes, as we shall presently examine this disease in detail.

It is apparent that jaundice in typhoid fever is not always associated with the same lesion, and that we can no more regard it as significant of any one hepatic disorder than we can jaundice met with in the varied diseases of the liver and bile passages unconnected with typhoid fever. Further on, I shall endeavor to make clear in how far we can, with reasonable certainty, distinguish between the different causes of jaundice in typhoid fever; but for the present I again state that the most frequent cause is from the blood infection, and without gross organic lesion, though in a moderate proportion of cases this exists.

Taking this general view of the subject, let us inquire into the gravity of the symptom. It is, indeed, a grave symptom, as may be judged from the following table, in which I have placed, together with my own cases, those in which there is sufficient detail to make them of any clinical value, and excluding the cases associated with perforation of the gall-bladder and other very marked gall-bladder lesions, which I shall speak of separately.

We have thus, in 52 cases, 33 deaths and 19 recoveries. Analyzing further these cases, according to their probable cause, we find them thus grouped: 4 catarrhal; 3 pylephlebitis, of which in one (the case of McPhedran) there were also marked changes in the liver; 5 of cholecystitis, in 2 of which (the cases of Sander and of Griesinger) there was most probably, too, cholangitis; 6 cases of abscess of the liver; 5 of acute yellow atrophy or a state closely akin to it (2 of Frerichs, 2 of Murchison, and 1 of Sabourin), and 29 cases in which blood infection and more or less of a fine parenchymatous change in the liver existed; of these, 5 (Sorel's) are not fully enough reported for us to be certain as to the cause of the jaundice, and, for the sake of accuracy, cannot be counted, leaving 24 in which the condition just mentioned was either proved or may be with reasonable certainty assumed to have existed. It would be very desirable to separate those in which there is a mere blood infection, induced by the presence of the typhoid bacilli or their toxins in the blood, or the absorption of septic matter with or without infected thrombi, and leading to alterations in the blood-corpuscles, from those in which decided, though not gross, parenchymatous changes happen. But it is impossible to do so with any certainty. Moreover, there is no fixed line; changes in the liver texture are soon secondarily induced.

Table of Fifty-two Cases of Jaundice Observed in Typhoid Fever, with Results.

No.	Author.	Reference.	No of cases.	Probable cause of jaundice.	Marked associate symptoms.	Result.	Post-mortem appearances.	Remarks.
1	Andral	Clinique Médicale, 1834, vol. i. pp. 10, 616.	2	Blood infection	In the first case pneumonia of left lung; heavy congestion of both lungs. In the second case jaundice very marked.	Died.	In both cases lesions of typhoid fever; condition of liver not stated in first case. In second nothing abnormal was seen in liver and biliary passages.	
2	Louis	Fièvre Typhoïde, 1841, vol. i. obs. xvii. p. 118, and obs. xxvi. p. 369.	2	Blood infection and liver abscess in first case; blood infection in second case.	In the first case suppurating parotid gland; pain in the sides and in epigastrium; bilious vomiting; marked delirium. In the second case jaundice on the twenty-fifth day of the disease, preceded by erysipelas of leg.	Died.	Typhoid fever lesions in intestines; enlarged mesenteric glands; an abscess near the free border of the liver; six smaller masses (metastatic abscesses?) in the small and middle lobes; bile passages healthy. In second case many typhoid fever ulcers; softened mesenteric glands; healthy liver and biliary ducts; distended gall-bladder.	
3	Frerichs	Diseases of the Liver, obs. xiii., 1858, obs. xviii.	2	Blood infection and parenchymatous change in liver (like acute yellow atrophy).	Great tenderness in region of liver, and afterward of entire abdomen; thin greenish stools; bilious vomiting: chill, dyspnœa. In the second case chill; thin, pale stools; violent epistaxis; tremor; dyspnœa; diminution of hepatic dulness.	Died.	Typhoid ulcers in ileum; débris of disintegrated cells, oil globules in the portions of softened liver; liver yielded leucin and tyrosin abundantly; gall-bladder not affected. In the second case liver shrivelled; disintegrat'n of hepatic cells, some filled with fat; mucous membrane of gall-bladder not affected; small quantities of whitish fluid in gall-bladder.	
4	Sander	Deutsch. Klin., 1861, p. 70.	1	Cholecystitis and probably cholangitis.	Jaundice appeared at end of second week; became very marked; vomiting; grayish stools; severe pain like bilious colic; tenderness in hepatic region and enlargement of liver; after five or six days gradual disappearance of the jaundice.	Died.	Biliary ducts were found to be dilated, and a large number of stones were in the gall-bladder.	After having entered on convalescence, the patient died in the eighth week subsequent to double parotitis.
5	Chvostek	Med. Chirurg. Rundschau, June, 1861, p. 188.	1	Blood infect'n; liver abscess.	Laryngeal perichondritis; deep jaundice; abscess of lung; pneumothorax	Died.	Two large abscesses in liver, evidently pyæmic and secondary; also abscess in left lung.	

6	Burder	Lancet, Oct. 17, 1874.	1	Blood infect'n; liver abscess.	Icterus on sixth day of fever in a boy nine years of age; greatly increased after a chill on the eighth day; liver dulness normal; diarrhœa.	Died.	The liver was a mass of small abscesses; superficial ulceration of Peyer's patches.	Had the bath treatment; death on seventeenth day of the disease.
7	Heitler	Wien. med. Presse, 1875, No. 3.	1	Blood infect'n; parenchymatous change in liver.	Date of beginning of fever uncertain; jaundice probably about third week, preceding diarrhœa; stools bilious, subsequently yellow; no chills; urine albuminous, also blood and tube-casts in it; normal liver percussion; increasing jaundice; delirium; coma.	Died.	Ulcers in ileum; lungs congested; liver rather large, flabby, soft; brown bile in gall-bladder; spleen enlarged to four times its normal size.	
8	Sidlo	Der militär Arzt, Wien, 1875, No. 23, p. 20.	1	Abscess of liver.	Pain in the hepatic region on thirty-second day of typhoid fever; on thirty-fifth day jaundice; swelling of liver; abscesses over right mastoid, in right temple, and in right axilla; tumor there gradually shrank; great emaciation; gradual diminution of liver dulness and of jaundice.	Recov.	.....	Abscess of liver discharged through bowel, pus and blood passing by the bowel on eighty-fourth day, after severe abdominal pain; complete recovery by one hundred and twentieth day.
9	Griesinger	Infectionskrankheiten; detailed also by Hagenmüller, Thèses de Paris, 1876, No. 269.	1	Cholecystitis with probable cholangitis.	Woman, aged twenty, in sixth week of typhoid fever, peritonitis, icterus, chills; painful tumor to right of umbilicus; swelling of liver; great prostration; convalescence. In eighth week return of tumor, with chills, icterus, vomiting; got better; subsequently two more relapses; the symptoms disappearing under treatment with large doses of opium. Final recovery in fifth month.	Recov.	.....	The patient had previously had jaundice several times, especially at her periods. The case is remarkable for its length, the recurrence of the symptoms, and the final recovery.
10	Laveran	Case communicated to Hagenmüller and published by him, Thèses de Paris, 1876, No. 269.	1	Cholecystitis.	Repeated bilious vomiting, severe pain in right hypochondrium, which is painful; icterus slight; fever reaching 40.6° C.; considerable prostration; no tumor mentioned.	Recov.	....	Symptoms came on in sixth week, early in convalescence.
11	Goltdammer	Deutsch. Arch. f. k. Med., 1877, vol. xx. p. 68.	2	First case most likely from blood infection and parenchymatous change. Second, catarrhal; but not fully enough reported to be certain.	Tenderness and swelling in hepatic region in one case of severe typhoid fever; no details given of second case except that the jaundice was of short duration and occurred in convalescence.	Recov.	.....	Very meagre details given. In both cases the bath treatment had been employed.

No.	Author.	Reference.	No. of cases.	Probable cause of jaundice.	Marked associate symptoms.	Result.	Post-mortem appearances.	Remarks.
12	Murchison	Diseases of the Liver, 2d ed., 1877, Cases CXXXVII., CXXXIX. Two mentioned (p. 401) without being described. One case (under Rostan's care) communicated (CXXXVIII.).	5	One catarrhal (CXXXVII.); one blood infection (CXXXIX.); in the other two blood infection & parenchymatous changes; in the communicated case this also most likely cause.	In first case clay-colored stools; no hepatic tenderness; constipation; jaundice occurred in a relapse; case recovered. In Case CXXXIX. jaundice appeared on fourteenth day associated with albuminuria, subsequent thrombosis, jaundice passed away; death from gradual exhausion. In two cases no particulars. In communicated case jaundice persisted during convalescence.	3 died. 2 recov.	In two cases liver found to be small, and its secreting cells loaded with oil.	
13	Petrina	Prag. med. Wochen., 1881, Nos. 41-43.	4	Case I. Blood infection, pylephlebitis with thrombi, miliary abscesses in liver.	Severe typhoid case; jaundice appeared thirteenth or fourteenth day of disease, not preceded by chill, and gradually increased, becoming very deep; fever high (highest 40.6° C.), with marked morning remissions and evening exacerbations; profuse sweating; moderate meteorism; liver enlarged and sensitive, left lobe especially; stools yellowish-brown or brown; profuse diarrhœa toward end; bile-pigment but no albumin or sugar in urine.	3 died. 1 recov.	Fresh and old cicatrizing lesions in Peyer's patches; lungs congested; liver very large, full of yellow points, which are found to be miliary abscesses; granular and fatty changes in hepatic cells; thrombosis of some of the finer portal veins; dark bile in gall-bladder; spleen large; in pancreas a few yellow foci; lungs congested.	
				Case II. Blood infection, probable parenchymatous change in liver.	Icterus eighteenth day of disease; repeated chills; marked fluctuation between morning and evening temperature; liver enlarged; whole region sensitive; vomiting and epigastric pain; profuse sweats; no albumin in urine; ascites; congested lungs, œdema of lungs.	.....	.....	No autopsy. The marked gastric symptoms and the occurrence of ascites are remarkable features of this case, which was probably one of pylephlebitis.
				Case III. Probable parenchymatous change.	Jaundice on fifteenth day, preceded by chill on thirteenth; abdomen sensitive, especially liver region over left lobe; liver increased in size; urine contains bile-pigment, no albumin; chills recur. Patient left the hospital improving, but still jaundiced; the liver and spleen were still swollen after nearly four weeks.	.....	.....	Though not specifically stated, it is likely that this patient recovered.

				Case IV. Cholecystitis, with cholangitis; interstitial hepatitis.	Jaundice on second day of a typhoid fever relapse; jaundice preceded by chills; liver enlarges, becomes tender on pressure; bilious stools, subsequently yellow; repeated chills; apparent recovery, except slight jaundice and enlarged liver remaining. Returns to hospital, a little over a month after leaving it, with œdema of lower extremities; yellowish, liquid stools; urine full of bile-pigment; general dropsy develops, with hydrothorax and ascites, and abdomen is tapped; dies of œdema of the lung after a lingering illness.	.....	Cicatrized Peyer's patches; thickening of mucous coat of gall-bladder; peritoneal adhesions between stomach and liver; liver small, surface granular; biliary ducts in liver filled with brownish-yellow masses, some containing spear-shaped concretions, others fibrinous coagula; some of the smaller bile-ducts have undergone obliteration with increase of connective tissue; this process also spread to Glisson's capsule, and led to atrophy of the liver; thus interstitial hepatitis had occurred following inflammation of gall-bladder and bile-ducts; cholelithiasis accedens is also recorded.	
14	Sabourin	Revue de Méd., 1882, p. 600.	1	Parenchymatous change (acute yellow atrophy).	Man, twenty-nine years of age; deep jaundice preceded by epistaxis; time of appearance of jaundice uncertain; meteorism, diarrhœa, delirium, albuminous urine, intestinal hemorrhage; average temperature 39° to 40.6° C.; pain on pressure in right iliac fossa and right hypochondrium.	Died.	In intestines ordinary typhoid fever lesions; heavy congestion of lungs; liver diminished in size in a state of acute atrophy with fatty degeneration of the hepatic cells; gall-bladder contained a small amount of almost healthy-looking bile.	
15	Stedman	Med. and Surg. Rep., Boston City Hospital, 3d ser., 1882.	1	Parenchymatous change in liver.	Jaundice, probably early in second week; tenderness in right hypochondrium; no epistaxis, nausea, or vomiting; urine, besides bile-pigment, contains a trace of albumin; diarrhœa, hypostatic congestion of lungs; highest temperature recorded 102°.	Died.	Liver enlarged and of nutmeg appearance; Peyer's patches swollen, not ulcerated; spleen softer but small; kidneys enlarged and in a state of cloudy swelling.	This case is not free from doubt as one of typhoid fever. Death occurred on the eighteenth day, and Peyer's patches should then have shown ulceration.
16	Freundlich	Deutsch. Arch. f. klin. Med., 1883, Bd. xxxiii. p. 318.	1	Blood infect'n; pyæmia.	Jaundice early in fifth week of typhoid fever, in which thrombosis of the scrotal veins followed by gangrene there and in the inguinal region had arisen; repeated chills; in the progress of the case persistent albuminuria and intestinal hemorrhages.	Died.	Anatomical lesions of enteric fever in intestines; double croupous pneumonia of lower lobes; condition of liver not stated.	Death in middle of fifth week.
17	Mathieu	Revue de Méd., July, 1886, vol. vi. p. 633.	...	.....	.....	.....	....	Very doubtful case, in which at end of the second week temperature became 38° C. Was it abortive typhoid followed by a relapse?

No.	Author.	Reference.	No. of cases.	Probable cause of jaundice.	Marked associate symptoms.	Result.	Post-mortem appearances.	Remarks.
18	Sorel	Bull. et Mém. de la Soc. Méd. des Hôpit. de Paris, 1889, vol. vi. 3d ser., p. 224.	6	Cannot judge from slight description.	Four cases happened at beginning of the malady, two of which were fatal; one case jaundice shortly before death; one in convalescence. In one case, p. 239, epistaxis was frequent.	3 died. 3 recov.	.....	No particulars given, except that in one case in which there had been also bloody urine, the liver was said to have been altered.
19	Romberg	Berlin. klin. Wochenschritt, March, 1890.	1	Blood infect'n; thrombosis of vena porta, and small liver abscesses.	Intestinal hemorrhage; albuminous urine; chill on twenty-fourth day of the disease; next day jaundice; brownish or yellow soft stools, sensitive abdomen, increased liver dulness and tenderness in hepatic region; fever with irregular remissions; icterus became intense; repeated chills. Death on thirty-first day of disease.	Died.	Many typhoid ulcers, for the most part in the process of healing; phlegmonous suppuration in mesentery near cæcum; thrombi in ileocæcal vein and its branches; liver markedly enlarged and full of small abscesses, especially of left lobe; masses of staphylococci in thrombi in portal veins.	
20	McPhedran	Canadian Practitioner, March, 1891.	1	Blood infection and parenchymatous change (diffuse pylephlebitis).	Symptoms came on, in a man, as convalescence was about to set in; temperature became irregular; recurring chills with sweating; jaundice; increase of liver dulness. Subsequently signs of chronic peritonitis.	Died.	At autopsy, diffuse pylephlebitis and chronic purulent peritonitis found; in the mesentery a small abscess apparently originating in a mesenteric gland.	
21	Jamieson	Imperial Maritime Customs, China Med. Reports, 1888–95, 37th issue, pp. 63, 67.	9	Blood infection with probable parenchymatous change.	Jaundice appeared in one case on the fifth day, in one on the eighth, in three on the tenth, and one respectively on the eleventh, fourteenth, seventeenth, and forty-fourth days; deep jaundice in all, and symptom not of gradual onset.	4 died. 5 recov.	.....	Four of the five cases in which jaundice appeared before the eleventh day proved fatal. Severe intestinal hemorrhage occurred in three of the fatal cases.
22	Lannois	Rev. de Méd., 1895, p. 911.	1	Parenchymatous change; cholecystitis.	Icterus began toward third week of severe typhoid fever; at first light, it became very intense, black; liver greatly enlarged, marked meteorism, intense pulmonary congestion. Death eleven days after appearance of icterus; not long before, a superficial abscess appeared on back of hand, and one on the internal surface of the leg on the same side.	Died.	Many Peyer's patches involved. Enormous liver, weighing 3000 grammes, yellow and fatty; gall-bladder greatly distended, containing, besides a clear liquid, flocculent muco-pus; superficial erosions in membrane; biliary passages, no ulceration or abscesses.	This was a very marked case of suppurative cholecystitis.

23	Osler	Transactions of Association of American Physicians, 1897.	2	Catarrhal in first case; blood infection (with parenchymatous change?) in second.	In the first case nausea and vomiting came on early in a relapse of typhoid fever, of which the original attack was one of moderate severity; jaundice appeared fourth day of relapse; no enlargement of liver; tenderness on deep pressure in front of tenth rib; nausea and vomiting prominent symptoms; profuse sweats; clay-colored stools; temperature range from 102° to 103.5°. In second case severe attack of typhoid fever; jaundice at end of second week; jaundice became of considerable intensity; meteorism; abdomen not tender; liver dulness not decreased; marked delirium; nystagmus: temperature, which had been high (105°), dropped to 97.2°.	1 recov. 1 died.	.....	In the second case the patient died on the sixteenth day. It was remarkable that, notwithstanding a falling temperature for four days, the pulse was of good volume.
24	Da Costa	Present paper.	5	1 catarrhal; 1 pylephlebitis; 3 parenchymatous changes in liver with blood infect'n.	Detailed in present paper. Jaundice marked in all.	3 died. 2 recov.	....	All were severe cases of typhoid fever.

Looking at the results, according to the best-ascertained cause of the jaundice, we note in the four catarrhal cases three recoveries and one death, this being the catarrhal case of my series, which, however, died a considerable time after the disappearance of the jaundice. In the three cases of pylephlebitis we find one recovery and two deaths; in the five cases of cholecystitis with jaundice there were two recoveries and three deaths; in six cases of abscess of the liver, one recovery and five deaths; of the five cases of yellow atrophy all died.

The most common of the ordinary and lighter changes in the liver structure consists in a cloudy swelling, with granular degeneration in the hepatic cells. But Handford,[1] while mentioning that both parenchymatous and interstitial changes are frequently found, regards as the most constant and, perhaps, the most important of these, interstitial hepatitis. This may, as a sequence, lead to atrophic cirrhosis, as in a case reported by Bourdillon.[2] The little opaque areas of destroyed liver-cells, that were formerly described as lymphoid nodules, and are not uncommon, do not, so far as is known, give rise to any symptoms pointing to the necrotic change.

The question may arise whether the jaundice may not be due to some agent employed in the treatment. But it has been observed under the most diversified, including the cold bath, treatment.[3] Werner,[4] who is an advocate of the use of chloroform in typhoid fever, states that he observed jaundice in four cases, very light in three, without swelling or tenderness of the liver, and stopped the remedy. But in six other cases treated with chloroform later, also in boys under fifteen years of age, notwithstanding the longer use of the remedy, jaundice did not occur.

Jaundice in typhoid fever happens most often at the *age* at which typhoid fever usually happens. But Petrina[5] reports a case in a woman aged fifty-six years; Burder,[6] one in a boy aged nine years. I do not know of a single instance in early childhood. As regards *sex*, many more cases have been met with in men than in women.

The main object of this paper is the consideration of the clinical significance of jaundice in typhoid fever, and this has now been done. But it would be incomplete without inquiring into the frequency with which jaundice is absent, though hepatic complications exist, and with-

[1] Hepatitis in Enteric Fever. Trans. Path. Soc. London, 1889.
[2] La Semaine Médicale, September 30, 1891.
[3] Goltdammer mentions two such cases. Deutsch. Arch. f. k. Med., 1877, Bd. xx. p. 68.
[4] St. Petersburger med. Wochenschrift, 1892, p. 32.
[5] Prager med. Wochenschrift, 1881, Nos. 41 and 43.
[6] Lancet, October 17, 1874, p. 552.

out a consideration of the character of these complications. Of the relative importance of these, we may get a fair idea by examining Hölscher's statistics in 2000 fatal cases of typhoid fever at the Pathological Institute of Munich.[1] Among 227 involving the liver and gall-bladder, there were 203 of disease of the liver structure; 12 cases of abscess; 3 of acute yellow atrophy; 1 of amyloid degeneration of the liver; 5 of diphtheritic processes in the gall-bladder and suppuration, including one of perforation of the gall-bladder; 3 of œdema of the gall-bladder; while 22 in addition are classed simply as icterus, without being linked to any organic disease.

The ordinary parenchymatous alterations, that are presumably represented by the 203 in the numbers just quoted, are not to be recognized during life, and force themselves on our attention only in the few instances in which they are attended with jaundice; the very great majority of the changes in the liver structure in typhoid fever give rise, indeed, to no symptoms. Leaving for separate consideration diseases of the gall-bladder, *abscess* of the liver is the affection which most often manifests itself. Yet it cannot be said that abscess of the liver in typhoid is often met with. Hölscher's statistics have just been quoted. Romberg mentions 677 cases with 88 deaths, among which there was but one liver abscess; it was associated with suppurative pylephlebitis. Schultz[2] analyzed 3686 cases with 362 deaths, without a single instance of hepatic abscess.

As regards abscess of the liver, I have collected twenty-two cases in which the association with typhoid fever seemed beyond doubt, and which admit of more or less complete clinical analysis. Others that have been reported I have rejected as very uncertain, as the combination with typhoid fever is not proved. Bouillaud's case, mentioned by Andral,[3] which has been questioned, I have included. Of the 22 cases, 7 only had jaundice; in 3 it is specifically mentioned as not present, and in 12 it is not mentioned at all, making 15 cases out of 22 in which jaundice may be fairly presumed to have been absent. Thus jaundice is not a symptom to be depended on in the diagnosis of abscess of the liver in typhoid fever. More important are chills, violent, prolonged, and repeated, as in Barth's[4] case, and generally preceding the jaundice, should this happen, as in Romberg's case; great variations in temperature, as in Case I. of Petrina; profuse sweating and sensitiveness in the region

[1] Münchener med. Wochenschrift, January, 1891, Nos. 3 and 4.
[2] Observations made at the Hamburg Hospital, quoted by Romberg, loc. cit.
[3] Clinique Méd., 3d edition, 1834, vol. i. p. 616.
[4] Bull. de la Soc. Anat., 1853, p. 80.

of the liver. The liver may or may not be swollen; in Goltdammer's case it was swollen. In Gerhard's[1] case the right hypochondrium was prominent, and tender on pressure, and fluctuation was detected over the right lobe of the liver. As further symptoms pointing to abscess of the liver, should there be any hepatic manifestations, are abscesses in other parts of the body, as in the parotid (Louis's case), in the perichondrium of the larynx (Chvostek's case), over the mastoid region (Sidlo's case). At times hepatic symptoms are wholly wanting, and the abscess is only found at the autopsy.

All the symptoms mentioned may also happen in pylephlebitis, except the rarest, fluctuation; especially the repeated chills, the pain and tenderness in the hepatic region, the high irregular temperature; and I know no way of distinguishing pylephlebitis from abscess, with which, indeed, it is generally classed, unless by the progress of the case, in which enlargement of the subcutaneous abdominal veins and collections of fluid in the peritoneum may be observed in addition. But the latter signs occur to a decided extent only where there is also marked thrombosis in the portal veins or its main branches, as in a case of Lannois,[2] and there is apt to be painful enlargement of the spleen as well as of the liver. I think jaundice, most probably pyæmic and from infected thrombi, is apt to happen among the symptoms of pylephlebitis with greater frequency than in abscess of the liver not associated with this, and to become deeper; but it is far from invariable. It was absent in the case of Asch and of Bernhard,[3] an instance of pylephlebitis from suppurating glands in the mesentery, and where there was a purulent thrombosis of the mesenteric veins and the venæ portæ were full of pus.

Viewed in its clinical bearings, we find abscess of the liver in typhoid fever under these conditions: as metastatic abscess, due to a pyæmic infection from other parts of the body, as the consequence of pylephlebitis, which is nearly always caused by an infection from typhoid lesions in the intestine, or from suppurating mesenteric glands and a resulting infective thrombosis; or, as owing to typhoid ulceration in the biliary passages and secondary suppuration. The first of these causes is illustrated by most of the cases in the table, notably by those of Louis, of Chvostek, of Sidlo, of Dunin,[4] of Barth.[5] To the second category belong the cases of Lannois, of Osler, of Romberg, of Gerhard,[6] of

[1] Medical News, July 24, 1886.
[2] Revue de Médecine, 1895, p. 913.
[3] Berlin. klin. Wochenschrift, 1882, xiv. p. 772, and Jahrb. für Kinderheilkunde, N. F., 1886, Bd. xxv.
[4] Deutsch. Arch. f. k. Med., 1886, Bd. xxxix. p. 379.
[5] Bullet. de la Société Anat., 1853, p. 80.
[6] Loc. cit.

Tüngel,[1] in which pus from a suppurating lymphatic gland near the cæcum broke into a root of the superior mesenteric vein; of Bückling[2] with a similar history; of Asch and Bernhard,[3] where there was also a suppurating mesenteric gland. Cases belonging to the third group are the rarest. A very striking one is mentioned by Klebs,[4] in which a suppurative inflammation of the bile passages within the liver happened, and their dilatation formed abscesses filled with thick, greenish, muco-purulent liquid. In the pus from liver abscesses, typhoid fever bacilli were found by Lannois. It may be also a question whether in some of the cases regarded as metastatic there have not been separate foci of inflammation and suppuration due to the typhoid bacilli; for instance, in the cases in which the parotid glands, as well as the liver, have been implicated.

In this connection we may discuss whether there be a form of typhoid fever in which liver symptoms arise, including jaundice, owing to the direct action of the specific micro-organisms on the liver or the bile channels. Mathieu[5] describes, under the title of "typhus hépatique benin," a case which he believes to have been of this character, and in which a relapse similar to a typhoid fever relapse happened, and Pfuhl[6] cites nine cases that came on after swimming repeatedly in a swimming school in the infected Elbe water at Altona near Hamburg, and all of which had fever and jaundice. I have analyzed these cases, and do not find their clinical history closely corresponding to typhoid fever. They all recovered, and are spoken of as due to mixed infection. Mathieu's case also recovered; and, as these cases happened before the introduction of the Widal test, we must remain in doubt as to their nature. I had at the Pennsylvania Hospital last year a case of jaundice in a colored woman (Case No. 2775), with fever, violent epistaxis, hebetude, diarrhœa, and albuminous urine, in which the Widal test gave positive reactions. She had been suffering with fever for two weeks, and it preceded the jaundice. The case proved fatal in the third week of the disease, and seemed to be an undoubted one of typhoid fever with hepatic complication. At the autopsy no lesion was found in the intestinal glands. The mesenteric glands were here and there enlarged, and one appeared as if it had pressed upon the choledoch duct; the gall-bladder was much distended, and its mucous coat inflamed; the liver was small and in a high state of fatty degen-

[1] Thierfelder, Ziemssen's Handb., Bd. viii. p. 84.
[2] 36 Fälle von Leberabscess, Berlin, 1868.
[3] Loc. cit.
[4] Handbuch der pathol. Anat.
[5] Revue de Méd., July, 1886.
[6] Deutsch. milit. arztl. Zeitsch., 1898, vol. xvii. pp. 9, 10.

eration; the spleen was small; the kidneys large, with signs of interstitial nephritis. Unfortunately, through a misunderstanding, no cultures were made from the liver and gall-bladder, as had been intended, and, notwithstanding the positive character of the Widal test, I hesitate greatly to bring forward the case as one of hepatic typhoid without intestinal lesion; it may have been one of acute yellow atrophy, of which it presented also many of the symptoms.

More common in typhoid fever than diseases of the liver itself are the diseases of the bile passages. We know through recent researches how frequent is their infection, especially the gall-bladder infection, with the typhoid bacilli. Chiari[1] reports the results of autopsies in twenty-two patients, and only in three was the bacillus absent from the gall-bladder. In twelve cases there was inflammation of the mucosa alone; in one the whole wall was affected, causing peritonitis.[2] In the discussion that followed a valuable paper by Mason,[3] on "Gall-bladder Infection in Typhoid Fever," Councilman stated that he had found the typhoid bacillus in nearly every case. Gilbert and Girode[4] demonstrated the presence of the typhoid bacillus in suppurative cholecystitis. Dupré[5] got pure cultures of typhoid bacilli from the gall-bladder of a patient operated on for gallstones six months after typhoid fever; in another case, in a man who died about the fifteenth day of typhoid fever, although the gall-bladder presented no obvious pathological changes, pure cultures of Eberth's bacillus were obtained.

Not only do these gall-bladder infections happen in the course of typhoid fever in association with the characteristic intestinal lesions of the disease, but they have been observed when these were absent. Cases of the kind are reported by Guarnieri[6] and in most interesting papers by Osler[7] and by Cushing.[8] Mark Richardson's[9] case, in which there was no distinct history of typhoid fever, but in which the typhoid bacillus was found in the fluid obtained from the distended gall-bladder by operation, is another case in point. It is quite as likely that the infection of the gall-bladder occurs in these instances through the typhoid bacilli in the blood as by direct infection from the continuous intestine. Further, great interest is attached to these gall-bladder infections in typhoid

[1] Eleventh Intern. Med. Congress, Zeitschr. f. Heilkunde, 1894, Bd. xv. S. 199.
[2] Case described, Prager med. Wochenschrift, 1893, No. 22.
[3] Transactions Assoc. American Physicians, 1897.
[4] Mém. de la Soc. de Biologie, 1890 and 1893.
[5] Infections Biliaires, 1891.
[6] Contrib. alla patog. della infez. biliari.; also, Baumgarten's Jahresbericht, 1892, S. 234.
[7] Trans. Assoc. American Physicians, 1897.
[8] Bulletin of the Johns Hopkins Hospital, vol. ix. No. 86.
[9] Boston Medical and Surgical Journal, December 16, 1897.

fever from the now established fact that they lead to the formation of gallstones; as, on the other hand, gallstones seem to invite the bacillary infection to the gall-bladder. The association with gallstones is curiously illustrated in a case by Chantemesse,[1] in which living typhoid bacilli were found in a gallstone removed by operation eight months after an attack of typhoid fever. Van Dungern's[2] case of bacilli found fourteen years and a half after typhoid fever in the pus from an abscess formed around the gall-bladder is unique; here, however, no stones were detected. The patient recovered.

Now, from the frequency, it might almost be said constancy, with which infection of the gall-bladder happens in typhoid fever, it would be supposed that symptoms referable to it are very common. But it is just the reverse. In the cases of irritation or the lighter cases of inflammation produced by it, there are absolutely no symptoms; even in the more severe cases, in which obvious lesions are found, symptoms are often absent or, at least, not recognizable; and thus the majority of cases pass undiscovered and mostly unsuspected. It is only the very marked ones, and chiefly those in which perforation has happened, that have been noticed. I shall attempt an analysis of such of the cases as have been published with sufficient fulness to give real information, and which seemed to me to be undoubtedly linked to typhoid fever, for it is astonishing in how many instances the evidence concerning this is most meagre. I have been greatly aided in the task by the courteous permission of Dr. Westcott to make use of the references he had prepared for the remarkable work of Dr. Keen, *On the Surgical Complications and Sequelæ of Typhoid Fever*, and by the most efficient assistance of Dr. Woodbury. After rejecting all the doubtful cases, I got together and tabulated fifty-three cases of cholecystitis in typhoid fever, some simple though marked, some suppurative, some perforative. But before analyzing these, it may be well to inquire in what proportion these affections have been noticed by pathologists irrespective of, as well as with, typhoid fever. Courvoisier[3] gives us valuable information on this point. Of 16 cases of cholecystitis of catarrhal origin or with beginning suppuration, fully 5 occurred in the course of typhoid fever. Six cases out of 55 of empyema of the gall-bladder were due to infection, one of which was from typhoid; 41 were due to cholelithiasis. In 7 cases of phlegmonous infiltration of the walls of the gall-bladder, typhoid was twice the cause, and the other 5

[1] Traité de Méd., tome i. p. 764.
[2] Münch. med. Wochenschrift, 1897, No. 26.
[3] Casuist. Statistische Beiträge z. Path. u. Chir. der Gallenwege, Leipzig, 1890, pp. 76–94.

cases were due to cholelithiasis. Fatal result is the rule in purulent cholecystitis. Of 82 cases, 53 proved fatal. Among these were 10 cases due to typhoid. In many of the cases there was no suspicion of cholecystitis prior to the autopsy. In cases of perforation of the gall-bladder, with encapsulation into the abdominal cavity, mentioned by Courvoisier, there were four in which no calculi existed, and which were due to typhoid.

Cholecystitis in typhoid fever, when at all marked, is a grave complication, no matter what be its exact form. In 58 cases of typhoid cholecystitis I have collected, there were 39 deaths and 15 recoveries, while in 4 the result was uncertain or not stated. Of the different forms, the instances of perforation without operation are the most fatal; 1 only out of 24 recovered by a discharge through the abdominal walls (case of Salzman); 3 recovered after operation (cases of Alexieef, Williams and Shield, Osler and Halsted). In suppurative cholecystitis there are a number of recoveries, but also as the result of operation (cases of Caspersohn, Mason, Richardson, Williams and Shield, Osler and Halsted). In the cases of cholecystitis which are catarrhal, recovery is not infrequent; where there is also cholangitis (as in Case IV. of Petrina and in Sander's case), the prognosis is not good. But Griesinger's case, in which this complication probably existed, recovered.

To proceed now with the clinical analysis of the 53 cases I have collected, to which, for some purposes, I shall add the 5 of cholecystitis with jaundice detailed in the table printed in this paper. Of these 58 cases there were 22 in which perforation of the gall-bladder happened. In 6 of the 22 cases of perforation gallstones were found, while in 16 they are either stated to be absent or are not mentioned; thus gallstones were not encountered in more than about one-fourth of the cases of perforation. Suppurative cholecystitis may, from the descriptions, be recognized in 24 of the 58 cases; and in eight of these there was also perforation. In the other instances the lesion was catarrhal, with very slight if any suppurative change. Ulcers of the gall-bladder cannot be absolutely separated from suppurative cholangitis, as in nearly all instances some suppuration coexists.

As regards *sex*, there is very little difference in the occurrence of the marked gall-bladder complications of typhoid fever. In 48 cases in which the sex is mentioned 26 were males, 22 females. The affections may be met with at almost any *age*. In 48 cases 8 were twelve years of age or less; 40 cases were over twelve years of age. The youngest

case happened in a girl, aged five years (case of Alexieef[1]); the oldest in a man, aged sixty-seven years (case of Anderson[2]).

The question of the *diagnosis* of these gall-bladder complications, and the possibility of telling them apart, is of great importance. It has been stated already that in many instances they are latent, and have only been discovered after death. But the knowledge of their occurrence, and the search for them in acute cases, will cause them to elude discovery less and less frequently. The marked symptoms are pain and tumor.

Pain is almost never absent. It is epigastric, or in the right hypochondrium, and is very often referred directly to the seat of the gall-bladder. It may be so severe that the patient shrieks, especially when he moves (as in Budd's case), or rolls in agony (Barthez and Rilliet's case). It often occurs in severe paroxysms. In the great majority of instances it is associated with marked tenderness, which, however, is not apt to remain confined to the region of the gall-bladder, but to be found also over the whole of the right hypochondrium or right side of the abdomen; and the entire abdomen even may be sensitive, most likely then from a spreading peritonitis. On the other hand, the general tenderness may become localized in the region of the gall-bladder. In a few instances sensitiveness, without pain, is spoken of; in a very few, as in a case of Louis', pain is mentioned as absent. Rigidity of the abdominal walls, especially on the right side, not infrequently coexists.

Tumor is of diagnostic significance as great as or even greater than pain, though it is not so common a symptom. It is specially mentioned in 21 out of 53 cases, only, therefore, in less than one-half. But it is probably present in larger proportion; the typhoid state of the patient and the marked meteorism that generally exists prevent its detection. It occupies the seat of the gall-bladder, and is thus to be looked for at Mayo Robson's[3] point, namely, at the junction of the upper two-thirds with the lower third of a line drawn from the ninth rib to the umbilicus. In a number of instances it is described as pear-shaped and firm, also as being tender on pressure; it may be a mere resisting mass below the costal margin. The tumor of the gall-bladder may be noticed to disappear slowly, or, where perforation happens, the disappearance may be sudden. In some instances the tumor swells up from time to time, as in the remarkable case of Leudet,[4] in

[1] Journ. Dietskaya Med., 1896, No. 4; abstracted in the American Journal of the Medical Sciences, October, 1897, p. 466.

[2] Medical News, August, 1896.

[3] Diseases of the Gall-bladder and Bile-ducts, 1897, p. 37.

[4] Clinique Médicale de l'Hôtel Dieu de Rouen, 1874.

which a woman who left the hospital apparently well, though with signs of a tumor from typhoid cholecystitis still perceptible under the false ribs, had markedly recurring swelling with tenderness at each menstrual period for six months. The tumor that is found, though having its origin in the lesion in the gall-bladder, may not be due to this viscus, strictly speaking, but, in the perforated cases, be a pus-cavity formed around it. The history of the case and the irregular shape of the swelling may lead us to suspect its cause, but there is no certainty in the discrimination.

Among the less marked symptoms are jaundice, nausea and vomiting, and chills. *Jaundice* occurred in 17 out of 58 cases, was thus absent or not mentioned in 41, and only occurs, therefore, in less than one-third of the cases. It is not, as a rule, deep, though, after it shows itself, it persists. It does not occur in the cases with perforation in any greater proportion; 5 only out of the 23 cases of perforation had jaundice. Nor is it of much more frequency in the suppurative cases, the proportion being 6 out of 24. Indeed, its relation to the gall-bladder lesions in typhoid fever is uncertain and of little value in diagnosis. In rare instances the jaundice is due to impaction of a gallstone, as in the case of Barbe,[1] in which attacks of gallstone colic and steadily deepening chronic jaundice preceded typhoid fever; and, at the autopsy, besides the characteristic intestinal lesions, a perforated gall-bladder was found and an obstruction of the common choledoch duct by a stone.

Nausea and *vomiting* occur as transient symptoms, though in much greater frequency than in the ordinary course of typhoid fever. They are mostly to be noticed at the beginning of the gall-bladder complication. In Legendre's[2] case the vomiting of large quantities of green, bitter fluid is specially mentioned. *Chills* are conspicuously absent. I find their occurrence noted in only 3 out of 54 cases, including the cases in which perforation happened. Burger's[3] case began with a severe chill; chills happened six days before death in Budd's[4] case, and happened also in one of Osler's cases. The other symptoms are those of severe cases of typhoid fever. But the frequent occurrence of pulmonary complications, especially toward the end of the fatal cases, is noteworthy. In a number of instances pneumonia was the immediate cause of death.

As regards the diagnosis of typhoid cholecystitis, this is impossible

[1] La France Méd., 1884, ii. p. 1071.
[2] Bull. de la Société Anatom. de Paris, 1881, p. 1893.
[3] Deutsch. Arch. f. k. Med., 1873, p. 623. [4] On Diseases of the Liver, 3d ed., 1857, p. 196.

with any certainty, except where tumor is present, though it may be suspected if there be nausea and vomiting, a sense of weight, and sensitiveness over the gall-bladder. But the occurrence of tumor and of pain and tenderness at or near the seat of the gall-bladder make the diagnosis not difficult. The most likely error is confounding the malady with an appendicitis. As a rule, the seat of pain and tenderness and swelling is different; in the one case in the right iliac fossa, in the other in the region of the gall-bladder. But we cannot trust implicitly to this; as in appendicitis, especially at its upper part, or where the appendix is not normally situated, the localization of the symptoms may be high up; and in cholecystitis the pain and tenderness may not be most marked over the gall-bladder, and the swelling may be very difficult to define.

An exact discrimination of the different forms of typhoid cholecystitis cannot be always made. They are all most likely to come on late in the disease, or after convalescence has been established, and all, whether with or without perforation, as Hagenmüller[1] has clearly established, are prone to be associated with local peritonitis in the neighborhood of the gall-bladder. Where there are abscesses in other parts of the body, and we can exclude pylephlebitis and hepatic abscess, a *suppurative cholecystitis* may be inferred, if pain and tumor be present. If there be a history of biliary colic and gallstone, or if this arise in the progress of typhoid fever or not long subsequent to it, signs of cholecystitis mean suppurative cholecystitis. I think, too, though there are not many observations on this point, that examinations of the blood will help us materially. We know through the researches of Thayer[2] that in typhoid fever the number of white blood-corpuscles varies but little from the normal standard, about 6000 per c.cm. Marked leucocytosis, if there be symptoms of cholecystitis, points to its being suppurative, as in Mason's case and in Anderson's case, where there was perforation. On the other hand, in a case of Osler's that recovered, there was no leucocytosis, and we may infer the cholecystitis not to have been purulent. In laying stress on leucocytosis we must, however, exclude abscess of the liver, in which condition it may also exist. Yet here the local symptoms are different: there is less pain, no tumor over the gall-bladder, and in doubtful cases I should attach much importance to the occurrence of chills. The analysis in this paper has proved their extreme rarity in cholecystitis of any form, whereas they are very com-

[1] De la Cholecystite dans la Fièvre typhoïde. Thèses de Paris, 1876, No. 269.
[2] Johns Hopkins Hospital Reports, vol. iv.

mon in abscess and in pylephlebitis, as is sweating. In none of these conditions can we lay much stress on the presence or absence of jaundice. There are cases of gall-bladder affection in typhoid fever in which there is mere distention with bile or a watery fluid. Case IV. of this paper probably belongs to these. They have been supposed, as in the case of Dumoulin,[1] to be due to retention of bile owing to nervous disturbance attending the fever, analogous to the retention of urine; or they may be the result of obliteration of the cystic duct, as in a case of Louis,[2] where the bile in the distended gall-bladder had the appearance of urine, and the cystic duct was compressed by an enlarged lymphatic gland that surrounded it. No means exist of distinguishing these cases during life from acute cholecystitis, except it be by the absence of severe pain and very marked tenderness. Then it is likely that they are really instances of bacillary infection of the gall-bladder, and that the typhoid bacilli will be found in the fluid, only marked inflammation has not been induced.

Perforation of the gall-bladder has as its chief symptoms suddenly developed or intensified pain, collapse, and peritonitis. In some instances that have been reported there is also marked drop of temperature, as in the cases of Bonamy[3] and of Bond.[4] The effect on the tumor is often a decided lessening or a disappearance. Peritonitis, which may remain local, as in the case of Hawkins[5] and others, develops, and may lead to encapsulation of the discharged contents of the gall-bladder. On the other hand, a subsequent general peritonitis may occur. The course is often a comparatively slow one, two of the reported cases, Ranvier's[6] and Archambault's,[7] not dying until the twelfth day after the perforation.

It is evident how very similar the symptoms are to those of intestinal perforation. Gall-bladder perforation can be, indeed, distinguished only by the seat of the pain and the previous existence of the tumor. Should jaundice be present it would be an additional aid in discrimination. On the other hand, intestinal hemorrhages preceding the symptoms of perforation, and rapidly developing general peritonitis, belong more strictly to the intestinal lesion; local peritonitis in the upper part of the abdomen on the right side is more characteristic of gall-bladder perforation, as is a slower progress of the symptoms. Fall of temperature, too, attending the collapse, occurs much oftener in intestinal perforation in typhoid fever than in gall-bladder perforation in the same disease.

[1] Gaz. Méd. de Paris, 1848, p. 551.
[2] Fièvre Typhoïde, vol. i. p. 201.
[3] Gaz. Méd. de Nantes, 1890, p. 133.
[4] British Med. Journ., July 12, 1884, p. 67.
[5] Medico-Chir. Trans., vol. lxxx. p. 138.
[6] Bull. de la Soc. Anat., 1864, p. 433.
[7] Bull. de la Soc. Anat., 1852, p. 90.

The *treatment* of the jaundice attending these different hepatic affections will be guided by our recognition of the probable cause. Those which are due to blood infection and to the finer parenchymatous changes in the liver cannot be reached by any special treatment, which must be that of the grave underlying typhoid condition. I will, however, point out that two of my cases recovered while taking decided doses of mineral acids, and this was also the result in two of Murchison's cases. In abscess of the liver, as well as in pylephlebitis, large doses of quinine may be employed. In the ordinary form of cholecystitis, recovery has followed applications of leeches over the swelling, followed by poultices, as in Observation No. LXVIII. of Frerichs. Besides the general treatment of the typhoid state, attention must be paid to the character of the discharges from the bowels; when very dark and showing vitiated bile, small doses of mercurials should be given. Leudet's[1] case got well under calomel and under frictions with belladonna. The suppurative cases require support, and, as soon as we are reasonably sure of their character, surgical interference, the admirable outcome of which was seen in the cases of Caspersohn,[2] of Williams and Shield,[3] of Alexieef,[4] of Mason,[5] of Osler and Halsted,[6] of Mark and Maurice H. Richardson.[7] Among the perforation cases I know of only one recovery without operation, the case of Salzmann,[8] in which a discharge occurred through the abdominal wall. An operation alone promises success, and how well it may succeed is proved by the results of Williams and Shield and one of the cases of Osler and Halsted.

[1] Loc. cit. [2] Festschr. f. Fr. von Esmarch, 1893, p. 455, Kiel and Leipzig.
[3] Lancet, March 2, 1896.
[4] Journ. Dietskaya Med., 1896, No. 4. Quoted in The American Journal of the Medical Sciences, October 1897, p. 466.
[5] Trans. Assoc. American Physicians, 1897. [6] Ibid.
[7] Boston Med. and Surg. Journ., December, 1897.
[8] Med. Corresp. Würtemb. Arztl. Verein., 1870, xl. 84.